Retinal and Choroidal Changes in Patients with Systemic Arterial Hypertension

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Original Research Article

ABSTRACT

Aims: To evaluate retinal and choroidal changes in patients with systemic arterial hypertension using optical coherence tomography (OCT).
Setting: The study was performed in the outpatient clinic of Tanta ophthalmology Hospital.
Design: Prospective, cross sectional and controlled study.
Patients and Methods: Retinal and choroidal changes using spectral domain optical coherence tomography that includes the following parameters: central macular thickness (CMT), Subfoveal choroidal thickness (SFCT), and Retinal nerve fiber layer thickness (RNFL).
Results: The study comprised 10 eyes of healthy individuals without hypertension, 15 eyes of systemic hypertensive patients on beta blockers for more than one year, and 15 eyes of systemic hypertensive patients on calcium channel blockers for more than one year. This study showed There were statistically significant differences between the three studied groups as regards the mean central macular thickness (CMT). In this study, we found a statistically significant decrease in the mean subfoveal choroidal thickness (SFCT) from 247.40 ± 46.18 µm in group A (non hypertensive) to 195.63 ± 28.96 µm in group B (hypertensive patients on beta blockers for more than one year) and decreased to 203.10 ± 27.74 µm in group C (hypertensive patients on calcium channel blockers for more than one year). According to the retinal nerve fiber layer thickness (RNFL), our study showed (100%) were within normal thickness in group A (non-hypertensive), In group B (hypertensive patients on beta blockers for more than one year) Twelve eyes (40.0%) were

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within normal thickness, ten eyes (33.3%) had thinning inferior, and eight eyes (26.7%) had thinning superior. Eight eyes (26.7%) were within normal thickness, ten eyes (33.3%) had thinning inferior, four eyes (13.3%) had thinning superior, and eight eyes (26.7%) were borderline in group C (hypertensive patients on calcium channel blockers for more than one year).

Conclusion: Hypertension (HTN) has significant increase in the central macular thickness , lower SFCT and thinning in retinal nerve fiber layer thickness in all quadrants compared to normotensive individuals. Neither beta blockers nor calcium channels blockers have significant changes on these previous parameters changes.

1. INTRODUCTION

"Hypertension (HTN) is a medical condition in which the blood pressure in the arteries is persistently elevated. High blood pressure typically does not cause symptoms, long term high blood pressure however is a major risk factor for coronary artery disease, stroke, heart failure and vision loss" [1]. HTN affects several body systems such as cerebrovascular, renal, cardiovascular and retina [2].

Ocular damage as a result of HTN appears in 3 forms: choriodopathy, retinopathy and optic neuropathy. "Hypertensive choriodopathy occur later than retinal vascular changes of arteriolar narrowing and arteriovenous crossing changes" [3]. "The manifestations of choroidopathy include serous retinal detachment, Elschnig spots, and siegrist streaks" [4,5].

Spectral domain optical coherence tomography (OCT) is non invasive technique, that has become very important tool in diagnosis of hypertensive retinopathy and choriodapathy [6]. Retinal and choroidal changes in patients with systemic arterial hypertension using optical coherence tomography with EDI that includes the following parameters: Central macular thickness in µm (CMT), Subfoveal choroidal thickness in µm (SFCT), and Retinal nerve fiber layer thickness (RNFL).

This study was carried out to evaluate retinal and choroidal changes in patients with systemic arterial hypertension using optical coherence tomography (OCT).

2. SUBJECTS AND METHODS

This prospective, cross-sectional, controlled study was carried out on 40 patients attending the Ophthalmology outpatient clinic at Tanta Ophthalmology Hospital. The duration of the study extended for 12 months (from October 2020 to September 2021). The study adhered to the tenets of the Declaration of Helsinki and all patients signed a written informed consent to participate in the study and for publication of data before enrollment in the study after approval from the ethical committee, Faculty of Medicine, Tanta University.

2.1 Participants in this Study were Divided into Three Groups

Group A: Normal individuals with no hypertension.
Group B: Hypertensive Patients on beta blockers for more than one year duration.
Group C: Hypertensive Patients on calcium channel blockers for more than one year duration.

2.2 Patient's Inclusion in the Study was Accomplished According to the Following Criteria

1. Hypertensive patients receiving beta blockers and calcium channel blockers for more than one year.
2. Eyes with clear ocular media

The following cases were excluded from the study:

1- Diabetic patients and other systemic diseases that affect retinal and choroidal circulation.
2- Hazy media that will interfere with reliable OCT images.
3- Eyes with previous ocular surgeries.
4- Any local diseases including glaucoma

All patients included in the study were subjected to the following:

1. History taking:

Detailed history taking including anti hypertensive drug used:

- Generic name, trade name, type, number, dose and duration.
- Past history of any ophthalmic surgery, drugs or prior eye disease.

2. Full ophthalmic examination:

- BCVA.
- Anterior segment examination using slit lamp biomicroscopy with no abnormal data.
- Posterior segment examination using slit lamp biomicroscopy using auxillary lenses (90 diopter lens) and hypertensive changes in the form of generalized and focal arteriolar narrowing, copper wiring, and AV nicking were found in some patients.
- IOP measurement with applanation tonometry to exclude glaucomatous patients.

3. Investigations

- HBA1C and Fundus fluorescein angiography (FFA) were done to exclude diabetic patients.
- Optical Coherence tomography (OCT).

We used Heidelberg Engineering OCT Spectralis in this study with enhanced depth image mode to gain choroidal image.

2.3 Statistical Analysis

Statistical analysis was performed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. Shapiro-Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

The used tests were:

2.3.1 Chi-square test

For categorical variables, to compare between different groups.

2.3.2 Monte Carlo correction

Correction for chi-square when more than 20% of the cells have expected count less than 5.

2.3.3 Mann Whitney test

For abnormally distributed quantitative variables, to compare between two studied groups.

2.3.4 F-test (ANOVA)

For normally distributed quantitative variables, to compare between more than two groups, and Post Hoc test (Tukey) for pairwise comparisons.

2.3.5 Kruskal Wallis test

For abnormally distributed quantitative variables, to compare between more than two studied groups and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons.

3. RESULTS AND DISCUSSION

In group A(Normal individuals), included 5 females and 5 males. While group B(Hypertensive patients on beta blockers) included 6 males and 9 females, and group C(Hypertensive Patients on calcium channel blockers) included 6 males and 9 females. The mean age was 49.20 ± 6.09 years ranging from (41.0 – 60.0years), 55.53 ± 10.01 years ranging from (42.0 – 71.0 years), and 56.87 ± 6.76 years ranging from (47.0 – 72.0 years) in groups A, B, and C respectively (Table 1).

The mean duration of hypertension was 5.60 ± 2.92 years ranging from (2.0 – 10.0 years), and 8.20 ± 3.47 years ranging from (4.0 – 15.0 years) in groups B and C respectively. No statistically significant difference between the two studied groups (p= 0.051) (Table 2).

3.1 OCT Results

The mean central macular thickness was 238.95 ± 11.91 μm ranging from (212.0 – 255.0 μm), 274.33 ± 29.82 μm ranging from (184.0 – 331.0 μm), and 310.07 ± 50.47 μm ranging from (223.0 – 399.0 μm) in groups A,B, and C respectively. There were statistically significant difference between the three studied groups (p<0.001*). (Table 3) (Fig. 1).

The mean subfoveal choroidal thickness was 247.40 ± 46.18 μm ranging from (157.0 – 299.0 μm), 195.63 ± 28.96 μm ranging from (148.0 – 263.0 μm), and 203.10 ± 27.74 μm ranging from (160.0 – 299.0 μm) in groups A,B, and C respectively. There were statistically significant decrease between group A and B (p1<0.001*) and between group A and C (p2<0.001*). There

were no statistically significant difference between group B and C (p3=0.667). (Table 4) (Fig. 2).

As regard retinal nerve fiber layer thickness, Twenty eyes (100%) were within normal in group A. Twelve eyes (40.0%) were within normal thickness, ten eyes (33.3%) had thinning inferior,

and eight eyes (26.7%) had thinning superior in group B. Eight eyes (26.7%) were within normal thickness, ten eyes (33.3%) had thinning inferior, four eyes (13.3%) had thinning superior, and eight eyes (26.7%) were borderline. There were statistically significant difference between the three studied groups (p<0.001*). (Table 5) (Fig. 3).

Table 1. Demographic data

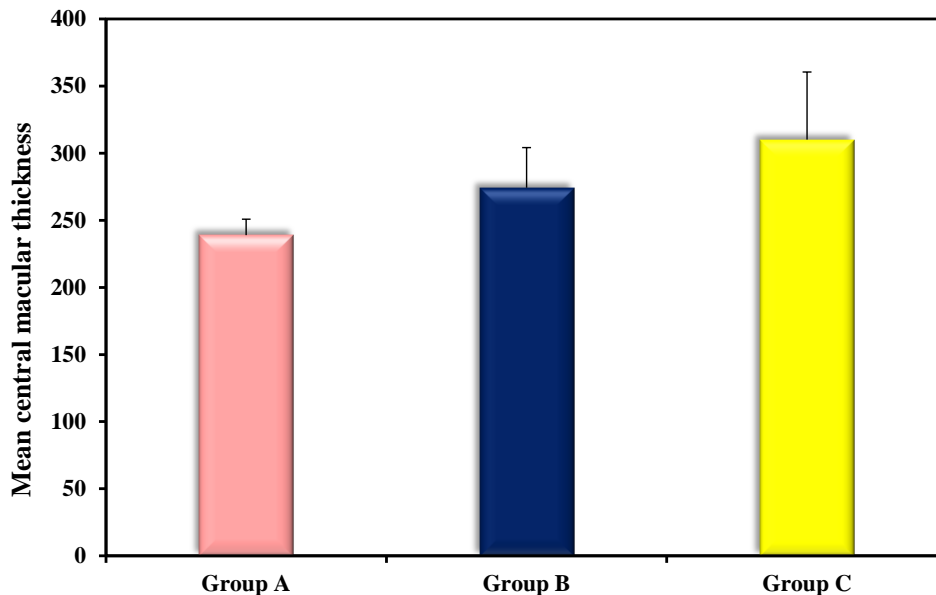|	Group A (n =10)		Group B (n =15)		Group C (n =15)		Test of sig.	P
	No.	%	No.	%	No.	%		
Gender								
Male	5	50.0	6	40.0	6	40.0	χ^2=0.307	0.858
Female	5	50.0	9	60.0	9	60.0		
Age (years)								
Min. – Max.	41.0 – 60.0		42.0 – 71.0		47.0 – 72.0		F=	0.064
Mean ± SD.	49.20 ± 6.09		55.53 ± 10.01		56.87 ± 6.76		2.964	
Median (IQR)	48.5 (45.0–54.0)		55.0 (47.5–64.5)		56.0 (53.0 – 61.0)			

Fig. 1. Central macular thickness

Table 2. Duration of hypertension and treatment in the two studied groups

	Group B (n =15)	Group C (n =15)	U	P
Duration of HTN				
Min. – Max.	2.0 – 10.0	4.0 – 15.0	65.50	0.051
Mean ± SD.	5.60 ± 2.92	8.20 ± 3.47		
Median (IQR)	5.0(3.0 – 7.50)	9.0(5.5 – 10.5)		
Duration of treatment				
Min. – Max.	1.50 – 5.0	2.0 – 6.0	66.0	0.056
Mean ± SD.	3.23 ± 1.27	4.20 ± 1.26		
Median (IQR)	3.0(2.0 – 4.50)	4.0(3.0 – 5.0)		

Table 3. Central macular thickness

Central macular thickness	Group A (n =20 eyes)	Group B (n =30 eyes)	Group C (n =30 eyes)	F	P
Min. – Max.	212.0 – 255.0	184.0 – 331.0	223.0 – 399.0	23.205*	<0.001*
Mean ± SD.	238.95 ± 11.91	274.33 ± 29.82	310.07 ± 50.47		
Median (IQR)	239.50 (234.50–247.0)	279.50 (265.0 – 289.0)	293.50 (278.0 – 357.0)		
Sig. bet. Groups	p_1=0.003*, p_2<0.001*, p_3=0.001*				

Table 4. Subfoveal choroidal thickness

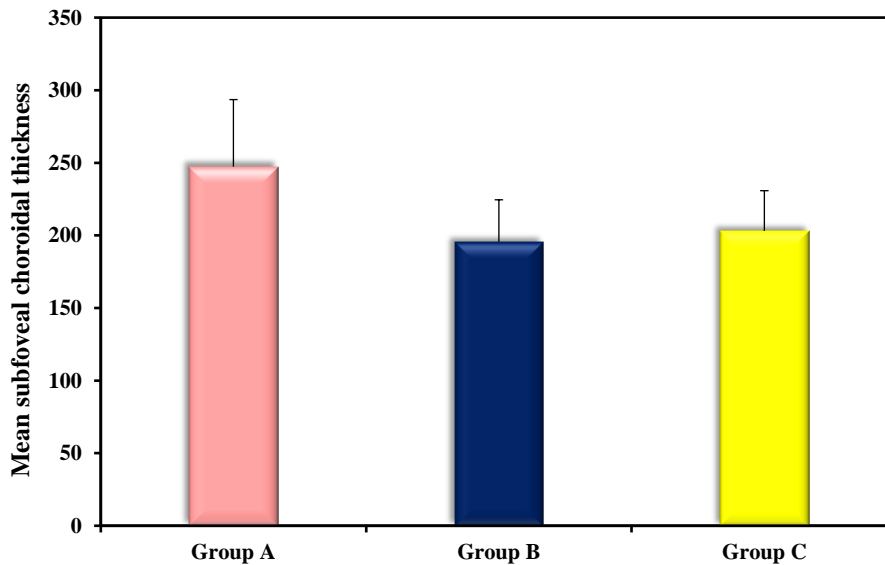| Subfoveal choroidal thickness	Group A (n =20)	Group B (n =30)	Group C (n =30)	F	P
Min. – Max.	157.0 – 299.0	148.0 – 263.0	160.0 – 299.0	15.658*	<0.001*
Mean ± SD.	247.40 ± 46.18	195.63 ± 28.96	203.10 ± 27.74		
Median (IQR)	254.50 (230.50286.50)	193.50 (178.0 – 211.0)	200.0 (188.0 – 219.0)		
Sig. bet. Groups	p_1<0.001*, p_2<0.001*, p_3=0.667				

Fig. 2. Subfoveal choroidal thickness

Table 5. Retinal nerve fiber layer thickness

RNFL thickness	Group A (n =20 eyes)		Group B (n =30 eyes)		Group C (n =30 eyes)		χ^2	^{MC}p
	No.	%	No.	%	No.	%		
Within normal	20	100.0	12	40.0	8	26.7	37.876*	<0.001*
Thinning inferior	0	0.0	10	33.3	10	33.3		
Thinning superior	0	0.0	8	26.7	4	13.3		
Borderline	0	0.0	0	0.0	8	26.7		
Sig. bet. Grps	$^{MC}p_1$<0.001*, $^{MC}p_2$<0.001*, $^{MC}p_3$=0.013*							

IQR: Inter Quartile Range, SD: Standard deviation, F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey), p: p value for comparing between the studied groups
*p1: p value for comparing between Group A and Group B, p2: p value for comparing between Group A and Group C, p3: p value for comparing between Group B and Group C, *: Statistically significant at p ≤ 0.05*
Group A: Normal individuals with no systemic hypertension, Group B: Systemic hypertension receiving beta blockers, Group C: Systemic hypertension receiving calcium channel blockers
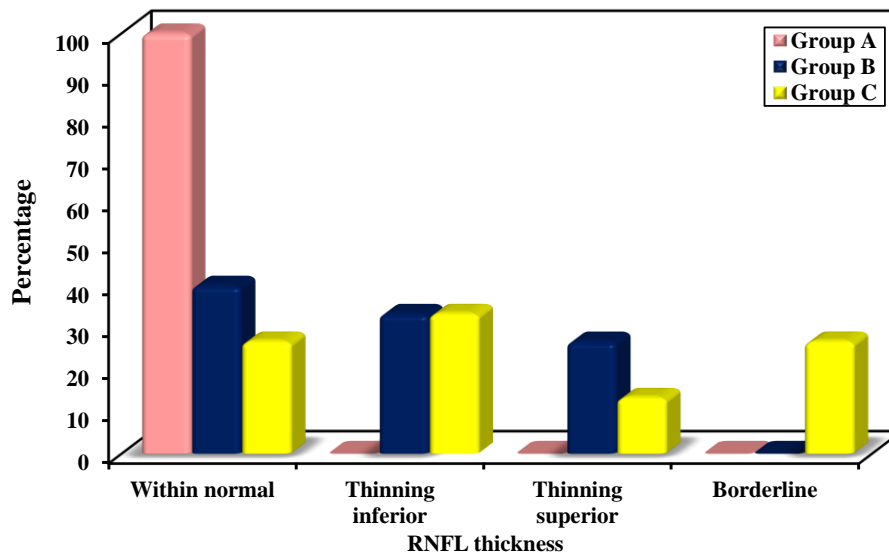
Fig. 3. Retinal nerve fiber layer thickness

4. DISCUSSION

This study aimed to evaluate the retinal and choroidal changes in hypertensive patients receiving treatment in the form of beta blockers or calcium channel blockers compared to normal control subjects using spectral domain optical coherence tomography with enhanced depth image to visualize choroidal thickness.

"Systemic arterial hypertension affects 25% of the world's adult population and is estimated to increase to 29% by 2025" [7]. "Approximately 90% of hypertensive cases are classified as essential hypertension, where the precise cause is unknown and it has widespread effects on the eyes" [8].

"Various changes in the eyes of hypertensive patients have been reported including retinopathy, choroidopathy, optic neuropathy, vascular abnormalities such as arterial and venous occlusive disease, retinal arteriolar macro aneurysm formation, and embolic events" [9].

"Systemic hypertension remains a major health problem worldwide with silent and multisystem complications" [9].

"Optical Coherence Tomography (OCT) is one of the most important non-invasive, reproducible and reliable ancillary tests for diagnosis of retinal pathology. It has allowed detailed quantitative analysis of retinal microstructure with high spatial resolution that has the advantage of segmenting the retina up to nine sector measurements rather than average thickness alone" [10]. OCT can be used for evaluation of the peripapillary retinal nerve fiber layer (RNFL), subfoveal choroidal thickness (SFCT) using EDI (Enhanced Depth Image) to visualize choroid, macular thickness and may provide a significant tool to detect ocular effect of hypertension and effect of therapy [11].

- Our study found that there was significant increase in the central macular thickness in group B and group C than control group. There was statistically significant difference between group A (control group) and group B (p1=0.003*), between group A and group C (p2<0.001*) and between group B and group C (p3=0.001*).
- This was similar to the study of Han-Min Lee, et al [12] which demonstrated that, at the time of initial diagnosis of hypertension, the mean central macular thickness in the hypertensive group were significantly greater than those of the control group. However longitudinal study of Han-Min Lee, et al [12]. found that the central macular thickness gradually and statistically significantly decreased with time mainly 1 year of follow up, stabilization of blood pressure and the disappearance of the retinal changes evident during the early period of elevated blood pressure.

- This disagree with the study of Lee et al. [12] which found that the central macular thickness was significantly thinner in hypertensive group than those of healthy eyes.
- Those results may be explained by the retinal swelling and optic disc edema induced by abnormally elevated blood pressure and failure of good control in most patients, and also the small sample size which hinder for further evaluation of cases..
- Regarding SFCT it was found that there is a decrease in the mean subfoveal choroidal thickness (measured by EDI OCT) in group B (hypertensive patients receiving beta blockers) and group C (hypertensive patients receiving ca channel blockers) than group A (control group). There was statistically significant difference between control group and hypertensive groups (p<0.001). There was no statistically significant difference between group B and group C.
- This results agrees with the study of Masís et al. [13] which demonstrated that the subfoveal choroidal thickness was significantly thinner in hypertensive patients compared to controls. Also a study of Akay et al. [14] demonstrated that "subfoveal choroidal thickness was significantly lower in hypertensive patients with respect to control subjects".
- This disagrees with the study done by Gök et al. [15] which showed that there was no significant correlation of the mean SFCT with hypertension.
- "Reduced SFCT may be explained by the choroid has one of the highest blood flow rates in the body [16]. Choroidal arteries have a unique course in the choriocapillaris. They run short with few branches and supply the choriocapillaris at right angles. Due to this architecture, high blood pressure is transmitted directly to the choriocapillaris" [17]. "The choriocapillaris is controlled primarily by the sympathetic nervous system, which in response to hypertension will cause vasoconstriction" [5,16] however, "the vasoconstriction may be overcome by a further increase in blood pressure that leads to muscle layer and endothelial damage" [5, 17]. In addition, "increased systemic arterial pressure and ophthalmic/ ciliary artery vaso-occlusion may result in choroidal ischemia [5] that may also contribute to choroidal thinning".

- Also in this study, neither beta blockers nor ca channel blockers had statistically significant difference on subfoveal choroidal thickness.
- As regard retinal nerve fiber layer, our study demonstrated that 40% of group B were within normal limits of thickness and 60% had thinning (mainly inferior and superior thinning), and group C had 26.7% within normal limits of thickness and 73.3% had thinning (mainly inferior, superior and borderline). There were statistically significant difference between the two hypertensive groups (p<0.001).
- This study agrees with Lee et al. study [18], that found that, "the hypertensive groups showed a significantly thinner RNFL than the control group. All four sectors in the HTN groups showed greater reduction rate in RNFL thickness than those in the control group. The superior and inferior sectors showed greater reduction rates than the nasal and temporal sectors in both groups". Also another study of Lee et al [12]. reported that "chronic hypertensive patients, even with well-controlled Blood pressure had a significantly thinner RNFL than normal controls". Also study of Akay et al. [14] found "significantly thinner RNFL thickness at average, superior and inferior quadrants in patients with systemic arterial hypertension".
- These results regarding RNFL thinning explained by retinal micro vascular changes caused by hypertension which are constriction or hardening of the retinal arteries [19].

In summary, hypertension was associated with increase in the mean central macular thickness compared to healthy controls. In addition, there was a significant decrease in SFCT in hypertensive groups than controls, and also there were statistically significant difference in retinal nerve fiber layer thickness between hypertensive and controls.

5. CONCLUSION

- The recent introduction of SD-OCT with EDI has enabled clinicians to evaluate a variety of ocular changes, associated with hypertensive retinopathy with detailed quantitative analysis of retinal microstructure with high spatial resolution.

Also we can detect improvement with treatment.

- Our study showed that anti hypertensive medication in the form of beta blockers or calcium channel blockers does not improve ocular changes associated with sustained hypertension because CMT slightly increased, SFCT slightly decrease and RNFL thickness decreased in comparison to normotensive patients.

CONSENT AND ETHICAL APPROVAL

The study adhered to the tenets of the Declaration of Helsinki and all patients signed a written informed consent to participate in the study and for publication of data before enrollment in the study after approval from the ethical committee, Faculty of Medicine, Tanta University.

ACKNOWLEDGEMENT

A brief acknowledgement section may be given after the conclusion section just before the references. The acknowledgments of people who provided assistance in manuscript preparation, funding for research, etc. should be listed in this section. All sources of funding should be declared as an acknowledgement. Authors should declare the role of funding agency, if any, in the study design, collection, analysis and interpretation of data; in the writing of the manuscript. If the study sponsors had no such involvement, the authors should so state.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/91318